

REMARKS

Reconsideration of the above-identified application is respectfully requested.

Claims 1-2, 4-9, 21-22 and 24-39 remain in this application. Claims 3, 10-20, and 23 have been canceled. Claims 1, 4, 5, 9, 21, 24-29, 31, 33, and 34 have been amended to more particularly point out and distinctly claim the subject matter that Applicants regard as their invention. Support for the amendment to claim 28 can be found on page 17, lines 13-17 of the specification. Claims 37-39 have been added to more particularly point out and distinctly claim the subject matter that Applicants regard as their invention. Support for claims 37 and 38 can be found in line 25 on page 12 to line 9 on page 13 of the specification. Support for claim 39 can be found on page 5, lines 23-25; page 6, lines 1-12; page 12, lines 6-25; and page 13, lines 1-11. No new matter has been added.

I. Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-9 and 27-28 were rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

With respect to claims 1-9 and 27, the Examiner quoted page 17, lines 8-12:

Formation of the multiplicity of particles as a thin film is a sensitive operation. In our experience, casting from solution with slow evaporation does not produce a thin film with reproducibility or acceptable uniformity. We have invented various methods that address this problem.

Based on this passage, the Examiner concluded that all methods of forming the composition do not result in an acceptable film or multiplicity of particles. Applicants respectfully submit that the Examiner mistakenly interpreted the word "acceptable" to modify

“film” and “multiplicity of particles,” while the Applicants clearly intended the word “acceptable” to only modify “uniformity.” It is obvious to those skilled in the art of chemical sensors that the quoted passage is referring to sensor-to-sensor device duplicability and that the word acceptable modifies only uniformity and only in the context of sensor-to-sensor device duplicability. On page 17, lines 13-25 and page 18, lines 1-19, two deposition methods are described that can be used to produce more uniform and reproducible films if many duplications of a single device are to be made with the requirement that each device respond to its environment in an identical manner.

Claims 1-9 and 27 are for an article of manufacture suitable for use in determining whether or in what amount a chemical species is present in a target environment, and claim 27 is for a method of fabricating an assembly suitable for investigation of a target environment to determine whether or in what amount a chemical species may be present. The invention, as defined in claims 1-9 and 27 is not dependent on a specific deposition method as long as the multiplicity of particles have the required close-packed orientation. The deposition method may become important for sensor-to-sensor device duplicability, as noted in the passage quoted by the Examiner. However, claims 1-9 and 27 are for either “**an** article of manufacture” or “a method of fabricating **an** assembly,” so they clearly are not describing sensor-to-sensor device duplicability.

Therefore, Applicants respectfully submit that the specification does enable a person of ordinary skill in the art to make and use the invention commensurate in scope with claims 1-9 and 27.

With respect to claim 28, the Examiner quoted page 22, lines 9-16 and relied on the process of making the particles found on pages 13-14 to assert that the process of claim 28 is not

supported by the specification. Claim 28 has been amended and is now supported by page 17, lines 13-17 of the specification.

II. Rejection under 35 U.S.C. § 102(b) – Bethell

Claims 1-5, 7-9, 21-27, and 33-34 were rejected under 35 U.S.C. § 102(b) as being anticipated by Bethell (J. Electroanal. Chem.).

To be anticipating, a reference must disclose every element of the claims. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991); *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989). If the reference lacks any claimed element, there is no anticipation. *Kloster Speedsteel AB v. Crucible Inc.*, 793 F.2d 1565, 1571 (Fed. Cir. 1986).

Bethell does not teach or disclose a ligand shell “of thickness from 0.4 to 4.0 nm” as recited in independent claim 1 (from which claims 2-5 and 7-9 depend), independent claim 21 (from which claims 22-24 depend), independent claim 25 (from which claim 26 depends), independent claim 27, independent claim 33, and independent claim 34. According to the specification (page 13, lines 12-17) of the present application, “[t]he shell is advantageously neither so thin that the multiplicity of particles is effectively metallic in its conductivity properties, nor so thick that the multiplicity of particles is completely electrically insulating. Preferably, such thickness ranges from 0.4 to 4 nm, especially 0.4 to 2.5 nm.” According to the Examiner, “Page 138, column 1, last full paragraph [of Bethell] teaches nonanethiol derivatized particles having a core diameter of 1.5-3 nm,” while this paragraph of Bethell actually states that “the metal particles had a narrow range of diameters in the range 1.5 to 3 nm.” The Bethell reference does not use the word “core” or the word “shell.” By changing the Bethell word “particles” to the word “core” with the attendant implication that the “shell” counterpart of the

invention is equivalent or anticipated by Bethell in his office action, the examiner is reading information into the Bethell reference that is not there. Although Bethell discusses particle core size, Bethell does not teach or disclose particles with a ligand shell of the required thickness. Therefore, Bethell does not anticipate claims 1-5, 7-9, 21-26, and 33-34.

Additionally, Bethell does not teach or disclose “a monofunctional ligand shell” as recited in amended independent claim 1 (from which claims 2-5 and 7-9 depend), amended independent claim 21 (from which claims 22-24 depend), amended independent claim 25 (from which claim 26 depends), amended independent claim 27, amended independent claim 33, and amended independent claim 34. Bethell uses the words “organic spacer” (page 137, top of right column) to describe the function of the organic components, which serves as “matrices” to embed metal particles (page 137, left column line 5) in his study. The Bethell concept for the “nonanethiol” and the “dodecanethiol” is that of a fixed organic spacer of different lengths, while the concept of the present invention is that of a monomolecular layer whose absorption and desorption of vapors results in a dynamic measurable property change. Bethell uses dithiols with bare clusters only for the purpose of providing an organic spacer or linker between neighboring gold particles as a way of making three-dimensional networks. Monothiols are not used by Bethell because they do not perform this function. In the present application, monothiols and other monofunctional ligand molecules are used to absorb analyte molecules.

The Examiner assets that there is a “significant similarity” between examples 26-30 of the present application and the process described by Bethell to form a self-assembled layered structure. Examining the details of Bethell reveals that a monofunctional alkanethiol (e.g. nonanethiol or dodecanethiol) is not used at all, and the clusters employed are those without the alkanethiol shell. In examples 26-30, all of the clusters have both a gold core and an alkanethiol

shell. This difference is significant as it requires knowledge that a ligand exchange action will occur for layered deposition of self assembled clusters. Bethell does not teach this knowledge.

Bethell uses dithiols and bare clusters (i.e. clusters without shells), while the present application teaches monofunctional ligand molecules to form the shell and the use of clusters with preformed shells in the synthesis of the self-assembled film. The specification of the present application clearly excludes dithiol for use in the ligand shell. The Bethell reference uses the descriptive term “organic spacer” and fails to use either “ligand” or “shell.” The “organic spacer” of Bethell serves a different function than that of a ligand shell.

Moreover, Bethell’s disclosure is not an electrical configuration for a sensing device and does not teach or disclose an article of manufacture, an assembly, or a system “capable of interacting with a chemical species in a target environment such that an electrical conductivity property of said multiplicity of particles is altered,” as recited in independent claims 1, 21, 25, 33 and 34. The objective of Bethell “was to develop materials in which it would be possible to control the transfer of electrons from one metal particle to another by controlling the size of the particles, their separation and, we hoped, the chemical nature of the organic spacers providing that separation. We had in mind particularly the possibility that, by incorporating into the spacers organic moieties that could be addressed electrochemically or photochemically, we could go some way towards the construction of electronic circuitry of a size range approaching the molecular.” (Page 409, col. 1-2) The focus of Bethell is on using only dithiols to link large bare clusters together for electronic circuitry. Throughout the reference, Bethell stays focused on its objective and in no way infers, speculates, or provides any means for anticipating that metal (gold or otherwise) nanoparticles with an appropriate ligand shell could be used for chemical detection as described in the claims of the present application. In fact, in the last paragraph of

the conclusion, Bethell speculates that “there are many applications for the nanostructured materials that have been described here. These range from submicroelectronic devices and circuitry (switches, diodes, electrochromics and photovoltaics) to electrical modification of the reflectance of glass.” Chemical sensors are not included in Bethell’s range of applications, and the configuration of this range of devices is not what one of ordinary skill in the art would select for a chemical sensor. Bethell does not teach an article of manufacture, an assembly, or a system “which is capable of interacting with a chemical species in a target environment such that an electrical conductivity property of said multiplicity of particles is altered” as recited in the amended claims of the present application. Therefore, Bethell does not anticipate claims 1-5, 7-9, 21-26, and 33-34.

III. Rejection under 35 U.S.C. § 102(b) – Andres

Claims 1-5, 7-9, 21-27, and 33-34 were rejected under 35 U.S.C. § 102(b) as being anticipated by Andres (“Self-Assembly of a Two-Dimensional Superlattice of Molecularly Linked Metal Clusters,” *Science*, Vol. 273, 1690-1698 (1996)).

The intent of Andres’ work was to explore a chemical self-assembly fabrication process that has relevance for nanoelectronic digital circuits. The design was to generate a two-dimensional planar array of regularly spaced metal nanoparticles of uniform size interconnected by rigid rod conjugated organic molecules. The approach was to prepare the bare clusters by gold evaporation and condensation, anneal to obtain a uniform size, coat with a dodecanethiol shell to obtain a solubilized cluster in aromatic solvents, spin coat from solution to obtain a monolayer array of regularly spaced dodecanethiol encapsulated gold particles, displace all of the dodecanethiol ligand shell molecules with rigid rod molecular wire interconnecting molecules (thiol or isocyanide terminated phenylenethylene trimers), and conduct electrical

measurements with a contacting electrode configuration that minimized the number of clusters in the electron transport path. TEM micrograph of monolayers of metal particle networks and nonlinear current-voltage characterization results are presented as evidence for the monolayer array fabrication and Coulomb blockade quantized effects on electron transport.

Andres does not teach or disclose a three dimensional assembly as recited in amended independent claim 1 (from which claims 2-5 and 7-9 depend), amended independent claim 21 (from which claims 22-24 depend), amended independent claim 25 (from which claim 26 depends), amended independent claim 27, amended independent claim 33, and amended independent claim 34. The present application clearly teaches a three-dimensional assembly of particles in close-packed orientation deposited onto a contacting electrode with varying degrees of coating thickness depending on the deposition method. In contrast, Andres goes to great lengths to accentuate the monolayer character of his deposition. Andres' teaching is limited to a "two-dimensional", "planar array" of metal particles. This teaching is reiterated many times in the Andres reference as evidenced by the following terms: "planar arrays" (abstract, p. 1690), "cluster monolayer" (abstract, p. 1690), "adjacent clusters in the monolayer to form a two dimensional superlattice of metal quantum dots" (abstract, p. 1690), "planar array of small metal islands" (middle column, p. 1690), "two-dimensional (2D) superlattice of uniform metal nanocrystals" (left column, p. 1691), "monolayer film of these coated particles" (left column, p. 1691), and "close-packed monolayer arrays" (page 1692).

Additionally, Andres does not teach or disclose a ligand shell "composed of an encapsulating monomolecular layer of ligand molecules each molecule having a single bonding site to a gold surface" as recited in amended independent claim 1 (from which claims 2-5 and 7-9 depend), amended independent claim 21 (from which claims 22-24 depend), amended

independent claim 25 (from which claim 26 depends), amended independent claim 27, amended independent claim 33, and amended independent claim 34. There is an important issue with regard to the nature of the ligand molecule interaction with the gold surface of the cluster core. With specific regard to employment of an alkyl thiol (dodecanethiol), Andres teaches the following (bold font added for later referral): "... a surfactant that rapidly **adsorbs** onto the surface of the clusters and prevents aggregation. A number of molecules have been found effective in this regard, including fatty acids, alkyl thiols, alkyl disulfides, alkyl nitriles, and alkyl isonitriles." (page 1691, bottom of right column); "... 1- to 5-nm diameter gold clusters **encapsulated** by 1-dodecanethiol are stable in mesitylene or decane for more than 6 months." (page 1692, left column); "... dodecanedithiol-**encapsulated** gold clusters ..." (Fig. 3 caption); "... the clusters are **surrounded** by a monolayer film of dodecanethiol." (page 1692, middle column). This verbiage (particularly use of the words adsorb, encapsulate, surround) is not equivalent to the teaching of claims 1, 21, 25, 27, 33 and 34 where, as expressed above, an "encapsulating monomolecular layer of ligand molecules each molecule having a single bonding site to a gold surface" is taught. This teaching is derived from the specification (page 12, lines 12 to 19), "The ligand molecule typically has a head-tail type structure; the head is a functional group possessing a bonding interaction with metal atoms in the core surface, and the tail has a structure and composition designed to provide additional stabilization of metal clusters (i.e. core bodies) against irreversible agglomeration, induce solubility in solvents and promote interactions with chemical species of interest." Andres' verbiage significantly changes when referring to the use of the aryl dithiol and aryl di-isonitrile molecules: "... it is possible to **covalently link** the clusters to each other using double-ended molecular interconnects ..." (page 1692, middle column); "Aryl dithiols and di-isonitriles completely displace alkyl thiols from a Au(111) surface

to form SAMs in which only one end of the molecule is **attached to the gold substrate** (12). These molecules also displace dodecanethiol from the gold clusters in an unlinked array and interconnect neighboring clusters to produce a **covalently linked** network.” (page 1692, right column). This latter verbiage indicates Andres teaches chemical bonding of aryl dithiols to the gold surface of a cluster, while Andres earlier verbiage above teaches adsorption absorption of alkyl thiol to the gold surface. The interactions of the aryl and alkyl thiols toward the gold surface are clearly different. Andres does not teach chemical bonding of the monofunctional alkyl thiol to the gold surface but does teach that the aryl thiol aggressively displaces alkyl thiol and bonds to the gold surface. Further, Andres teaches nothing about a free alkyl thiol or dithiol displacing an already adsorbed alkyl thiol from a gold cluster surface. Regarding the synthetic method to produce clusters, the Examiner states, “In the last full paragraph of the center column of page 1691, Andres teaches that the synthetic method used produces particle that are equivalent to those produced by the Brust method (see reference 5).” Andres actual wording here is, “... nanoparticles produced by this method are equivalent in quality ...” to the Brust method. What is meant by the words “equivalent in quality” is neither qualified nor defined.

Moreover, Andres’ disclosure is not an electrical configuration for a sensing device and does not teach or disclose an article of manufacture, an assembly, or a system “capable of interacting with a chemical species in a target environment such that an electrical conductivity property of said multiplicity of particles is altered,” as recited in independent claims 1, 21, 25, 33 and 34. Andres teaches the use of a large conjugated rigid rod double-ended molecular interconnect between metal particles with a molecular wire function (i.e. thiol or isocyanide terminated phenylenethylene trimers, page 1692, middle column) which is consistent with the stated objective of the reference, i.e., a proposed future basis for nanoelectronic digital circuits

(page 1690, third column). However, this is not the case for an invention involving chemical sensing where flexible coiled up chemical structures of the ligand shell molecules and of any intercluster self-assembly coupling agents is taught, and this is important in order to accommodate sorption of and swelling by analyte molecules. The resulting modulation of the distance between metal cores and of the dielectric character of the medium between cores caused by vapor absorption is central to the transduction for the sensing application but would have a detracting role in nanoelectronic circuitry.

In Andres, the number of metal particles involved in the electron transport measurement is minimized in order to obtain the nonlinear Coulomb blockade current voltage measurement. In the configuration normal to the planar array of particles, the contacting measurement is made by an STM probe through a single cluster (page 1692, third column), while in the configuration parallel to the planar array of particles, the contacting measurement is made by a thin (40-50 nm wide) line metal deposition with a 450 nm gap. In this planar configuration the current flows through a minimal number of individual clusters with a nonlinear dependence on voltage (page 1692-1693 and figure 5). In the present application, a planar configuration is used with an interdigital electrode. This maximizes the number of clusters through which electron transport occurs, provides greater signal to noise ratio in the form of higher measured currents and a simpler and more useful linear current-voltage dependence.

In summary, the features Andres' structure include a material makeup of a rigid rod linked cluster array, a constraining of the cluster array to two dimensions and a contacting electrode design that minimizes the number of clusters through which charge transport occurs. All of these features work toward making that overall structure inert to sensing the presence of any chemical species in its environment.

Therefore, Andres does not anticipate 1-5, 7-9, 21-27, and 33-34.

IV. Rejection under 35 U.S.C. § 103(a) – Bethell in view of Natan

Claims 2, 4, 6, and 22 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Bethell as applied to claims 1 and 22 above, and further in view of U.S. Patent 5,609,907 to Natan.

To establish a *prima facie* case of obviousness, the Examiner must show that one of ordinary skill in the art would have been motivated by the prior art to fashion an embodiment satisfying all claim limitations. *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974); M.P.E.P. 2143.03.

Like Bethell (as discussed above in section II of this Amendment), Natan fails to disclose a ligand shell with a thickness from 0.4 to 4 nm. The assemblies disclosed in Natan use large bare gold clusters that physisorb proteins such as streptavidin to achieve the non-covalent attachment of metal core particles. The proteins are very large molecules and, if used to coat a metal particle, would generate a shell so thick that each particle would be insulated from another and electron transport would not be measurable. Therefore, the hypothetical combination of Bethell and Natan does not disclose every claim limitation and, thus, does not render obvious claims 2,4, 6 and 22.

Moreover, like Bethell (as discussed above in section II of this Amendment), Natan does not disclose an article of manufacture or an assembly “which is capable of interacting with a chemical species in a target environment such that an electrical conductivity property of said multiplicity of particles is altered” as recited in the amended claims of the present application. The scope of Natan is limited to the preparation of self-assembled metal colloids as monolayer depositions primarily for the purpose of surface enhanced Raman spectroscopy (SERS) analytical applications. In Natan’s abstract, other applications are suggested (e.g., biocompatible surfaces, catalysts, nonlinear optics and electrochemical applications), but all prescriptions for

depositions of metal colloids use bare gold clusters and conform with a procedure dedicated to the SERS application. The scope and content of the art described in Natan is focused on the SERS application, which allows for optical sensing but not electronic sensing, and cannot accommodate an extension to a chemical sensing application as recited in the claims of the present invention. Therefore, the hypothetical combination of Bethell and Natan does not render obvious claims 2, 4, 6 and 22.

V. Rejection under 35 U.S.C. § 103(a) – Bethell in view of Terrill and Andres

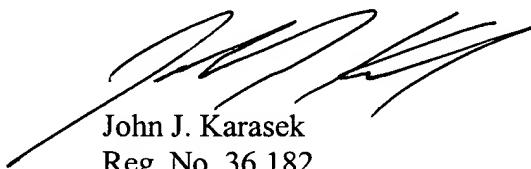
Claims 27 and 29-32 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Bethell as applied to claims 1-5, 7-9, 21-26, and 33-34 above, and further in view of Terrill and Andres. According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the electrodes and measurement apparatus of Terrill into the formation method of Bethell because of their known use and sensitivity for measuring resistivity of self-assembled colloid clusters as shown by Terrill. Additionally, the Examiner states that it would have been obvious to one of ordinary skill in the art at the time of the invention to use the ligand displacement method of forming the linked clusters in producing the layered structure of Bethell because of the greater flexibility in synthesis as taught by Andres.

Like Bethell (as discussed above in section II of this Amendment) and Andres (as discussed above in section III of this Amendment), Terrill is not an electrical configuration for a sensing device and does not teach or disclose a method of fabrication “capable of interacting with a chemical species in a target environment such that an electrical conductivity property of said multiplicity of particles is altered,” as required by independent claim 27 (upon which claims 29-32 depend). The electrical conductivity measurements in Terrill were made in a vacuum, which shows no anticipation of a sensor application. Moreover, in Terrill, electrical conductivity

measurements were made using very thick coatings. The coating deposition method of Terrill is a drop casting technique using a solution with a 100 mg/mL concentration that produces coatings of 2-20 μm thick, which is many times thicker than the height of the electrode. (Terrill last paragraph on page 2538) In the present application, it is explicitly stated that this technique is not adequate for a chemical sensing application and that acceptable "thin" film deposition techniques include spraying fine mist of a dilute solution onto a preferably heated substrate surface and chemical self assembly. (Page 17, line 8 through page 19, line 2) Therefore, the hypothetical combination of Bethell, Terrill, and Andres does not render obvious claims 27 and 29-32.

In view of the foregoing, it is respectfully submitted that this application is ready for allowance. Applicants respectfully request that a timely Notice of Allowance be issued in this case. Kindly charge any additional fees due, or credit overpayment of fees, to Deposit Account No. 50-0281.

Respectfully submitted,



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